Characterization of Dental Epithelial Stem Cells from the Mouse Incisor with 2D and 3D Platforms.

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Public Summary:
There are a large number of people who are missing teeth due to aging, trauma, or genetic factors. Regeneration of these tissues would be of great benefit to these patients. However, the ability to regenerate all of the tissues that make up a tooth is complex, due to the fact that there is a need for nerves, blood vessels, and two different cell types to make enamel and dentin, respectively. We have decided to focus on the regeneration of ameloblasts, the cells that make enamel. Humans lose these cells early on in development, but an attractive model to study these cells is the mouse incisor. These sharp, front teeth in mice are remarkable in that they grow continuously throughout the life of the animals, which is accomplished thanks to a pocket of adult stem cells that produce all the cells responsible for enamel formation. The goals of this paper were to develop tools to grow the mouse stem cells outside of the animal in order to better understand them. We were able to successfully culture these cells outside of the body for an extended amount of time. We also found several proteins involved in cell-cell adhesion as well as adhesion to the local microenvironment that could be used as potential markers to identify these cells more readily and that could give us information as to the specific environment suitable for maintenance of these cells. However, growing cells in a dish forces cells to experience a 2D environment, whereas cells in the body experience a 3D environment. To more closely mimic what the cells experience in the body, we successfully grew these cells in a 3D environment and found that the proteins expressed in the body were also expressed in the 3D culture system. Subsequently, we proposed to translate what we have learned from the mouse model into human cells by learning how to induce human embryonic stem cells, fetal cells, or adult cells to become tooth progenitor cells.

Scientific Abstract:
Dental epithelial stem cells drive continuous growth in the adult mouse incisor. To date, no robust system for the primary culture of these cells has been reported, and little is known about the basic molecular architecture of these cells or the minimal extracellular scaffolding necessary to maintain the epithelial stem cell population in an undifferentiated state. We report a method to isolate dental epithelial stem cells from the cervical loop of the mouse mandibular incisor. Cells were viable in a two dimensional (2D) culture system and did not demonstrate preferential proliferation atop various substrates. Characterization of these cells indicated that E-cadherin, integrin alpha-6, and integrin beta-4 mark the dental epithelial stem cells both in vivo and in vitro. We also grew these cells in a three dimensional (3D) microenvironment and obtained spheres with epithelial morphology and expression patterns. Insights into the mechanisms of stem cell maintenance in vitro will help to lay the groundwork for the successful generation of bioengineered teeth from adult dental epithelial stem cells.